

Dock No.: 263361US0PCT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF:

GROUP: 1623

Andrea CAPOCCHI

SERIAL NO: 10/516,945

EXAMINER: M.C. HENRY

FILED: August 23, 2005

FOR: A PROCESS FOR THE PREPARATION OF PIROXICAM: B-CYCLODEXTRIN INCLUSION COMPOUNDS

DECLARATION UNDER 37 C.F.R. § 1.132

COMMISSIONER FOR PATENTS
ALEXANDRIA, VIRGINIA 22313

Sir:

Now comes SCAPPATICCI GIUSEPPE who
deposes and states that:

1. I am a graduate of BIOLOGICAL SCIENCES and
received my / degree in the year 1976

2. I have been employed by INTERNATIONAL CHEMICAL INDUSTRY
SpA (ICI) for 31 years as a R&D DIRECTOR
in the field of CHEMICAL MANUFACTURING

3. The following experiments were carried out by me or under my direct supervision and control.

4. About 50 litres of water was poured into a tank and heated up to a temperature of 70-73°C.

5. 8.6 kg (7.57 moles) of β -cyclodextrin, 1 kg (3.02 moles) of piroxicam and 1 kg of 28% ammonium hydroxide were added in succession, and the mixture stirred for 30 min. The hot solution was poured through the tap on the temperature-controlled shelves of a freeze-dryer pre-cooled at -20°C.

6. By applying said temperature to the shelves, the solution reaches the freezing temperature of -10°C in 120 min, and hence at a cooling rate of about $0.7^{\circ}\text{C}/\text{min}$, so lower than $1^{\circ}\text{C}/\text{min}$.

7. Under these conditions of cooling, it has been observed that, when the solution reaches the temperature of $50-55^{\circ}\text{C}$, β -cyclodextrin begins to re-crystallize causing de-complexation of piroxicam.

8. Therefore pre-cooling the shelves of the freeze-dryer to a temperature of -20°C is not sufficient for achieving a cooling rate equal to or higher than $1^{\circ}\text{C}/\text{min}$, and hence for obtaining a product characterized by: i) completeness of the inclusion reaction; and ii) complete amorphization, and wherein piroxicam is present in the zwitter-ionic form.

9. The undersigned petitioner declares further that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of this application or any patent issuing thereon.

10. Further deponent saith not.

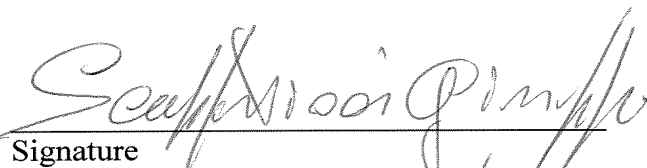
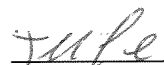
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Date